

THE BRADSHAW LECTURE

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E. A. TREVELYAN.



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# The Bradshaw Lecture

ENTITLED

## SOME OBSERVATIONS ON TUBERCULOSIS OF THE NERVOUS SYSTEM

*Delivered at the Royal College of Physicians of London  
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BY

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# The Bradshaw Lecture

ENTITLED

## SOME OBSERVATIONS ON TUBERCULOSIS OF THE NERVOUS SYSTEM.

MR. PRESIDENT AND GENTLEMEN,—My first duty is to acknowledge the honour done to me in asking me to give this lecture and to express the hope that I may prove worthy of it. I propose to address my remarks (1) to the forms which the tuberculous infection may assume in the nervous system; (2) to the mode of infection of the brain and meninges; (3) to some points in diagnosis connected with spinal puncture; and (4) to the possibility of recovery. I have to express my obligations to my colleagues on the staff of the Leeds General Infirmary for permission to use the records of 114 fatal cases which have occurred during the past 20 years in that institution. I must also thank Dr. Ursula Chaplin for much able help in laboratory work. To Professor S. Delépine and Professor G. Sims Woodhead, Mr. G. Dean of the Jenner Institute, and Dr. Steegmann of the Royal Commission on Tuberculosis I am indebted for some virulent cultures of the tubercle bacillus and to the last named also for valuable references.

### FORMS WHICH THE TUBERCULOUS INFECTION MAY ASSUME IN THE NERVOUS SYSTEM.

The various forms of tuberculosis of the nervous system consist of tuberculosis of the dura mater, tuberculous meningitis in its more general and limited forms, tuberculous masses in the brain and cord, and a possible miliary tuber-

culosis of the brain itself. An old question mentioned by Rilliet and Barthez<sup>1</sup> many years ago has been much discussed lately as to whether it is possible to have a tuberculous meningitis without the presence of tubercles, or at any rate with only a minimal tubercle formation. Such an affection has been compared to certain benign tuberculous affections of joints and serous membranes and the name of tuberculous meningopathy has been suggested to distinguish it from the ordinary fatal form of tuberculous meningitis. Poncet,<sup>2</sup> Patel,<sup>3</sup> Sepet,<sup>4</sup> and Galliard<sup>5</sup> are the chief exponents of this view and the subject has been well summarised by Bouclier<sup>6</sup> in a recent Lyons thesis. Among the 114 fatal cases at the Leeds General Infirmary there are 14 in which thickening or exudation is noted at the base of the brain without visible tubercles. Cerebral symptoms were present before death in 12 of these cases and abundant tuberculous lesions elsewhere in the body in all. I think it is fair to conclude that tubercle formation was at its minimum or even absent, at any rate in some of these cases, and that the changes noted were a manifestation of the tuberculous infection and were responsible for the symptoms. It has been suggested that the poisons of the tubercle bacillus may cause this more exudative or serous form of meningitis. Armand Delille has separated a poison which produced in his experiments productive tissue changes. On the other hand, the poisons of the tubercle bacilli injected intrameningeally may cause rapid death, as in Martin and Vandreuver's experiments.<sup>7</sup> Sicard<sup>8</sup> states that the tubercle bacillus and *its toxin* can produce exudation and granulations. In three instances of intrameningeal injection of measured quantities of tuberculin I found no local effects but progressive wasting ending in one guinea-pig in death. More information is obviously wanted about this benign form of tuberculous meningitis and its anatomical counterpart.

Occasionally in an ordinary tuberculous meningitis the

<sup>1</sup> Rilliet and Barthez : *Maladies des Enfants*, 1854.

<sup>2</sup> Poncet : *Bulletin de l'Académie de Médecine*, 1902.

<sup>3</sup> Patel : *Gazette Hebdomadaire*, December, 1902.

<sup>4</sup> Sepet : *Médecine Moderne*, 1902.

<sup>5</sup> Galliard : *Société Médicale des Hôpitaux*, 1902.

<sup>6</sup> Bouclier : *Thèse de Lyon*, 1902.

<sup>7</sup> Martin and Vandreuver : *Société de Biologie*, 1898.

<sup>8</sup> Sicard : *Ibid.*, 1898.

lesion is relatively a very limited one. Such cases have been recorded by Saenger<sup>9</sup> and in one case in my list the lesion was limited to one Sylvian fissure. But the limited meningitis described by French authorities (Chantemesse,<sup>10</sup> Combe,<sup>11</sup> Monnier,<sup>12</sup> and others) consists of a great thickening with tubercle formation over a limited portion usually of the motor cortex. It is said to occur in phthisis and its symptoms, as Combe points out, differ from those of ordinary tuberculous meningitis. There are nine cases in my series in which such localised thickening over a limited area of the cortex was noted. The most marked case was in a boy, aged seven years. The plaque occurred over Broca's convolution and difficulty in speech was noted during life. In this case there were miliary tubercles in the lung and in three other cases phthisis. This localised lesion may be produced experimentally (Sicard) and I have myself seen an instance of it.

Tuberculous masses in the brain are not infrequent. They were present in 33 of the 114 cases. In 15 they appeared to be recent and but little antecedent to the existing meningitis. In only 17 of the 33 cases were they multiple, a smaller proportion than usual. The largest number present in one case was four. In Middleton's case<sup>13</sup> there were 20, in Homen's case 12,<sup>14</sup> in West's case 12,<sup>15</sup> and in Henoch's case 12.<sup>16</sup> In size they vary from that of a millet seed to that of an orange and larger. They are mostly well defined and shell out with ease. Minute tubercles are often visible in the bed and on their surface, making recognition easy. They are often surrounded by an area of vascular engorgement but as a rule there is no definite capsule. They vary in consistency and when laid open display a yellowish and caseating centre and a peripheral growing zone made up of recent tuberculous tissue. Tubercle bacilli may or may not be found in this peripheral zone. As a rule, these masses show little tendency to break down and still less to calcify. They develop mostly in the grey matter and when they are situated more deeply they are often in relation with a

<sup>9</sup> Saenger : *Münchener Medicinische Wochenschrift*, 1903.

<sup>10</sup> Chantemesse : *Thèse de Paris*, 1884.

<sup>11</sup> Combe : *Revue de la Suisse Romande*, 1898.

<sup>12</sup> Monnier : *Thèse de Paris*, 1899.

<sup>13</sup> Middleton : *THE LANCET*, July 15th, 1893, p. 137.

<sup>14</sup> Homen : *Neurologisches Centralblatt*, 1892.

<sup>15</sup> West : *Transactions of the Pathological Society*, 1891.

<sup>16</sup> Henoch : *Vorlesungen über Kinderkrankheiten*, 1890.

process of the pia mater. Their favourite sites are the cerebellum, the pons, the crura, the cortex, and the central ganglia. Except in the pons, the medulla, and the cord, where they are usually surrounded by nervous tissue, they most often project on to the surface. The infection of the cerebro-spinal fluid is thus easily brought about as Ziegler<sup>17</sup> points out. Tuberculous tumours, indeed, sometimes give rise to no symptoms until this infection occurs. In 23 of my 33 cases there was present a tuberculous meningitis. In one of the cases there was a loose tuberculous tumour in the fourth ventricle. I have seen a section prepared from it by our pathological curator, Mr. J. A. Cairns Forsyth, and although there are no giant cells in the peripheral zone and no tubercle bacilli have been found, I do not doubt its nature. There were other tuberculous lesions in the body. Tuberculous tumours of the spinal cord are not common. Dr. A. G. Barrs had this drawing made of one and I have brought another specimen. It came from a child, aged three years, and there were other similar masses in the brain. Aniel and Rabot,<sup>18</sup> Müller,<sup>19</sup> Luce,<sup>20</sup> Gourand,<sup>21</sup> and Hunter<sup>22</sup> have recently related interesting cases of these tumours of the spinal cord.

In one of my cases an abscess possibly tuberculous was found in the pons along with tuberculous masses in the brain. Delafield and Prudden<sup>23</sup> state that these tuberculous masses may break down into abscesses. There is at present a beautiful specimen on view in St. George's Hospital museum, which shows multiple tuberculous masses breaking down into abscesses containing tubercle bacilli. The relatively rare tuberculous tumours of the dura mater are nearly invariably multiple and grow from its inner vascular surface in the posterior fossa or from the falx cerebelli. One of the two specimens from our museum came from a child, aged six years, with tuberculous cavities in the lungs, caseous bronchial and mesenteric glands, and intestinal ulceration. Miliary tubercles of the dura mater were noted twice, once by Dr. T. Wardrop Griffith, to whom I am indebted for many valuable comments upon the necropsies made by him.

<sup>17</sup> Ziegler: *Pathologische Anatomie*, 1901.

<sup>18</sup> Aniel and Rabot: *Lyon Médical*, 1898.

<sup>19</sup> Müller: *Deutsche Zeitschrift für Nervenheilkunde*, 1898.

<sup>20</sup> Luce: *Münchener Medizinische Wochenschrift*, 1903.

<sup>21</sup> Gourand: *Société d'Anatomie*, 1902.

<sup>22</sup> Hunter: *Brain*, 1902.

<sup>23</sup> Delafield and Prudden: *Pathological Anatomy*, 1902.



## MODE OF INFECTION OF THE BRAIN AND MENINGES.

It is admitted that a complete examination almost invariably reveals an older tuberculous focus somewhere in the body. In only six of my cases was no such focus found and here the notes are incomplete. Under congenital tuberculosis I need only refer to Demme's well-known and unique case<sup>24</sup> of a tuberculous cerebellar tumour in an infant, aged 23 days. If our knowledge of the infection of the meninges and brain were at all complete, which is by no means the case, we should know where the infecting focus is, what brings about the mobilisation of the tubercle bacillus from it, what channels the bacillus travels by, and what determines its settling down in any given area in the brain. The actual infecting focus may exceptionally be small and easily overlooked and it is obvious that the oldest lesion is not necessarily the infecting one.

A direct infection through the nose is believed to be possible, as in Demme's case quoted by Cornet.<sup>25</sup> A spread from tuberculous disease of the ear may take place; it is not quite direct because the ear would appear to be infected through the lymphoid tissue of the nasopharynx. Some recent experiments and observations tend, however, to show that the tonsils and the lymphoid tissue in the nasopharynx do not contain tubercle bacilli (at least virulent bacilli) as often as has been urged (Macfadyen and Macconkey<sup>26</sup> and Ito<sup>27</sup>). Grimmer,<sup>28</sup> who has worked at the subject, puts down tuberculosis as the cause of middle-ear disease in from 65 to 70 per cent. in children under five years and 16 per cent. above that age. There was obvious ear disease in ten of my 114 cases which were mostly admitted under the care of Mr. H. Secker Walker and Mr. A. L. Whitehead. Although the ear disease was not proved to be tuberculous it is interesting to note that in seven of these cases there was another old possibly infecting focus in the body and in another two the state of the glands is not noted. Experimentally I believe that it is very difficult to infect the brain and meninges through the accessory cavities. Again, in spinal caries I take it that a general tuberculous

<sup>24</sup> Demme: *Archiv für Kinderheilkunde*, 1881.

<sup>25</sup> Cornet: *Nothnagel's Specielle Pathologie und Therapie*, Band xiv.

<sup>26</sup> Macfadyen and Macconkey: *Brit. Med. Jour.*, 1903.

<sup>27</sup> Ito: *Berliner Klinische Wochenschrift*, 1903.

<sup>28</sup> Grimmer: *Laboratory Reports of the Royal College of Physicians of Edinburgh*, 1903.

meningitis is of infrequent occurrence. There are only four such cases in my series. In two the organs are said to be normal, in one the mesenteric glands are said to be enlarged, and in the other the glands are not noted at all. Miliary tubercles on the inner surface of the dura mater were noted in one case. In Dr. T. Churton's case of a large tuberculous tumour in the frontal lobes the spread from the bone to the dura mater and the brain seemed obvious, unlike a rather similar case recorded by Curtis and Booth<sup>29</sup> where the spread was said to be from within. Poli<sup>30</sup> suggests that the dura mater forms an important barrier against the spread from a neighbouring focus. In a single experiment devised to test this view I quite failed to confirm it.

The lungs were normal in 28 cases. It has been proved (as stated by Boinet<sup>31</sup>) that tubercle bacilli may pass through the lungs without leaving an obvious recognisable lesion. A miliary tuberculosis of the lungs was noted in 54 cases. 18 cases presented the lesions of phthisis, together with a miliary lesion in nine of them. Phthisis is said to be the most common cause of tuberculous meningitis in the adult. Personally I have had very little experience of this complication in obvious phthisis, although during the past four years I have had the opportunity of watching the course of phthisis in a considerable number of cases in connexion with the Leeds Tuberculosis Association. One case which I saw with Mr. B. Wainman I have reason to remember as I failed to assign the quite early vomiting to its proper cause. Among the cases of phthisis there was a child, aged six years, with one large cavity and several small ones. There are four other cases in children with recent cavitation which are not classed as phthisis.

Joints and bones were affected in 23 out of the 114 cases—viz., the hip in 13, the ankle in three, the knee, the elbow, and the wrist each in one case, and in four cases two joints were involved. The hip disease was old in two cases. Recently Courtin and Lourde<sup>32</sup> have described tuberculous meningitis in quite early hip disease. The small amount of tuberculosis noticed in the body in some of these joint cases was striking. The bones affected were the spinal column in four cases and the frontal bone and the ribs each in one case. In four cases the kidneys were the seat of extensive

<sup>29</sup> Curtis and Booth: *Annals of Surgery*, 1893.

<sup>30</sup> Poli: *Archives Internationales de Laryngologie, &c.*, 1903.

<sup>31</sup> Boinet: *Traité de Médecine*, Brouardel and Gibert, tome viii.

<sup>32</sup> Courtin and Lourde: *Journal de Médecine*, 1903.



tuberculous disease. It was associated in one case with pulmonary and laryngeal phthisis, in another with hip disease, and in a third with ear disease. The generative organs, no doubt not always examined, are noted as diseased in two cases, once in a man with a tuberculous testis and vas deferens and once in a woman with tuberculous Fallopian tube disease and tuberculous peritonitis. Simmond's statistics<sup>33</sup> show an extraordinarily high percentage. Thus in 60 cases of tuberculous meningitis one-third had genital tuberculosis. 35 of the 60 were men and here one-half were similarly affected. Ordinary tuberculous peritonitis was noted in eight cases and intestinal ulceration, mostly recent, in 28 cases. In another case there was extensive tuberculous ulceration of the colon and the rectum. Widenmann<sup>34</sup> reported a curious case of tuberculous meningitis in a man with primary ulceration of the intestine. In two of my cases there was an abscess about the vermiform appendix.

The relation of the lymphatic glands to tuberculous meningitis is of the first importance but unfortunately my records are distinctly incomplete in this respect. The lymphatic system constitutes a most important defence, especially in the child, against a general tuberculous infection. Manfredi and Fresco have been able to demonstrate even in so susceptible an animal as the guinea-pig the important rôle which the lymphatic glands play. There is a difficulty in connexion with these glands—viz., that they may contain virulent tubercle bacilli and yet appear as healthy to the naked eye. The glands which stand in the most direct relation to tuberculous meningitis are the mediastinal. Haushalter and Fruhinsholz<sup>35</sup> have recently found old and caseating lesions in the pretracheo-bronchial glands in 63 out of 67 cases of tuberculous meningitis. It is a particularly striking fact that in as many as 40 cases (35 with miliary tuberculosis) no old focus was present other than the adenopathy. This close relationship can only be connected with the all-important fact that the lungs constitute the port of entry of the tubercle bacillus in the large majority of these cases. Carrière<sup>36</sup> believes that the mesenteric glands may be the infecting focus in a goodly number of cases of tuberculous

<sup>33</sup> Simmond : *Münchener Medicinische Wochenschrift*, 1901.

<sup>34</sup> Widenmann : *Charité Annalen*, 1899.

<sup>35</sup> Haushalter and Fruhinsholz : *Archives de Médecine des Enfants*, 1902.

<sup>36</sup> Carrière : *Gazette des Hôpitaux*, 1902.

meningitis. It should be remembered that the infection of the mesenteric glands in a retrograde fashion from the mediastinal glands is obviously an anatomical possibility. We are obliged to appeal to this retrograde infection to explain some features in the spread of experimental tuberculosis. This mode of infection is more likely to be effective if there is any pressure upon the thoracic duct by enlarged and caseating mediastinal glands.

More puzzling still than some features connected with the infecting focus is the mobilisation of the tubercle bacillus from it. It has been suggested that tuberculin may bring about this effect. Rutimeyer's case<sup>37</sup> of phthisis in which tuberculous meningitis appeared at the close of a course of tuberculin treatment is very suggestive. I am aware that Cornet in his admirable work on tuberculosis will have none of this explanation. Simmonds<sup>38</sup> has seen cases of genital tuberculosis in which tuberculous meningitis ensued within from a few weeks to months after marriage. The occurrence of tuberculous meningitis shortly after an operation is a still more important matter. I have found eight cases of this class among the 114 cases. The interval between the operation and the meningeal infection forcibly reminds one of the incubation period in experimental tuberculosis. This interval has varied from one week to six or seven weeks; at least one case must be excluded as the interval is too short. The operations were upon the cervical glands, the ankle and the hip joints, also a laparotomy, &c. An absolutely satisfactory explanation is not forthcoming. Some have thought that tubercle bacilli have been liberated in the field of operation and have then gained access into the blood current. No doubt this view should receive practical attention. In the parallel case where an early phthisis blazes out after an operation into a fatal activity, of which I have recently seen two cases, one with Dr. Gordon Sharp, an explanation appears to me to be at hand. It may be attributed to an actual inhalation infection of hitherto sound parts of the lung brought about by the deep inspirations caused by the anæsthetic. Rhodonacki<sup>39</sup> has also recently published two cases of a fatal aggravation of the pulmonary lesion after operation. It has been suggested in cases of tuberculous meningitis following rapidly upon injury, as in a recent case by Mollard (quoted by

<sup>37</sup> Rutimeyer: *Berliner Klinische Wochenschrift*, 1891.

<sup>38</sup> Loc. cit.

<sup>39</sup> Rhodonacki: *Brit. Med. Jour.*, 1902.

Bouclier<sup>40</sup>), that the actual mechanical concussion may have led to escape of tubercle bacilli from the infecting focus but this explanation is not by any means convincing. There appears to be no satisfactory explanation of the occurrence of the disease at an interval after measles, whooping-cough, &c.

The route by which the bacilli travel from the infecting focus to the meninges or brain is far from satisfactorily worked out. It is either by the blood or the lymphatics. A striking fact in connexion with tuberculous meningitis is the marked alteration in the blood-vessels. In one case under the care of Dr. Barrs the Sylvian artery was blocked. Similar lesions have been recorded by several observers. In Cruchet's case<sup>41</sup> of at least a temporary recovery from tuberculous meningitis there were abundant old tubercles about the posterior cerebral and basilar arteries, the latter being almost occluded. In laying open the branches of the Sylvian arteries in one case I could see tubercles in the vessel walls. Sicard<sup>42</sup> has shown experimentally that the meninges may be infected, though with some difficulty, by injecting tubercle bacilli into the carotid artery; a pulmonary tuberculosis, however, is the common result unless the jugular veins are tied. Cornil, Bezançon, and Griffon<sup>43</sup> have studied the changes in the brain after injecting tubercle bacilli into the carotid artery of rabbits. No bacilli were found in the arterioles but they had multiplied in the perivascular sheaths which were filled with large swollen cells. The process illustrates according to the authors the development of tubercle at the expense of the lymphatic sheath. On the other hand, Sicard states as the result of his investigations that it is impossible to infect the meninges through the lymphatic system. These changes in the vessels, along with the experimental evidence, make it appear almost certain that the tubercle bacilli arrive by way of the blood stream. If they arrive in numbers they produce an ordinary general tuberculous meningitis, if few in numbers or perhaps attenuated they give rise to tuberculous tumours or even a meningitis *en plaque*—viz., an expression of a less virulent infection. Occasionally, and then I think only in the pons, the tuberculous tumour may look as if it had been formed, or was forming, by the coalescence of several foci of infec-

<sup>40</sup> Loc. cit.

<sup>41</sup> Cruchet (continuation of Rocaz's case) : *Revue Neurologique*, 1902.

<sup>42</sup> Sicard : *Presse Médicale*, 1900.

<sup>43</sup> Cornil, Bezançon, and Griffon : *Société d'Anatomie*, 1898.

tion. Broca and Souques<sup>44</sup> endeavour to explain the frequency of tuberculous tumours in the paracentral lobule (and Dr. Churton<sup>45</sup> some years ago recorded a well-marked case of the kind) by the rich vascular supply and the slowing down of the blood current here. It is curious that the lesions of the ordinary tuberculous meningitis should usually focus themselves chiefly about the middle cerebral artery and its branches, whereas tuberculous tumours are more frequently found in the distribution of the basilar and posterior cerebral arteries.

### EXAMINATION OF THE SPINAL FLUID.

Undoubtedly a most important addition to our resources in diagnosis consists in the examination of the cerebro-spinal fluid obtained by Quincke's spinal puncture. During this year I have examined the fluid from five cases of tuberculous meningitis. In one case, that of a boy, aged eight years, in the infirmary, whom I saw by the kindness of Dr. C. M. Chadwick, there was a pleural effusion present when the cerebral symptoms supervened. Ten cubic centimetres of clear fluid were drawn off. It contained a faint cloud of albumin and in the deposit lymphocytes alone were found and no tubercle bacilli. A small quantity of fluid, less than two cubic centimetres, injected subcutaneously tuberculised a guinea-pig. Another case, seen with Mr. H. J. Roper of Leeds, occurred in a boy, aged seven years, who had just passed through an attack of scarlet fever. The urine contained albumin and the vomiting in the very early days suggested a uræmic origin for the symptoms. On the second occasion on which I saw him there was a slight facial paralysis and the nature of the case seemed obvious. The clear spinal fluid contained very little albumin; the deposit showed many polymorphonuclear cells but no tubercle bacilli were found. The inoculation test gave a positive result. In a third case, that of a girl, aged four years, whom Mr. Norman Porritt of Huddersfield asked me to see, lymphocytes were present but no tubercle bacilli were found in the fluid. The inoculation test also gave a positive result. In another infirmary case the fluid was obtained after death. Albumin was present

<sup>44</sup> Broca and Souques : *Ibid.*, 1891.

<sup>45</sup> Churton : *Brit. Med. Jour.*, 1891.



and lymphocytes were found in the deposit but no tubercle bacilli. A quite recent case occurred in a lad, aged 16 years, whom I saw with Mr. D. McCann and who was transferred to the infirmary under my care. He was punctured at my request by Mr. G. W. Watson, our resident medical officer, on three separate occasions and 15, 35, and 13 cubic centimetres respectively of spinal fluid were drawn off. On the second occasion the pressure (four and a half inches in terms of the fluid) was estimated by Krönig's apparatus. Death occurred about the seventeenth day. There was miliary tuberculosis of the meninges, the peritoneum, and the upper lobe of the left lung. The bronchial glands were caseating and the mesenteric glands were enlarged. The spinal fluid was clear with a few small flocculi in it on two occasions and on the third it was more straw-coloured. It was slightly alkaline and contained a considerable amount of albumin (3 per 1000 Esbach). The specific gravity was 1006; the cellular elements were few but consisted solely of lymphocytes. Some of the fluid was incubated at 37° C. after Langner's method and flocculii were withdrawn from time to time and examined but no tubercle bacilli were found. One cubic centimetre was inoculated upon serum agar and glycerine agar respectively. About 2·5 cubic centimetres were injected subcutaneously, two cubic centimetres intraperitoneally, and about one cubic centimetre intrameningeally into guinea-pigs. Three tests were made with a view of comparing the results, as there has been some discussion about the best method. (As yet there has been insufficient time to obtain results from the culture and inoculation tests.) The cryoscopic point was 0·53, as against 1·03 obtained from some hydrocephalic fluid which was in my laboratory. The chlorides (one estimation) were 0·177 per cent. as against 0·223 (five estimations) of hydrocephalic fluid. The permeability test was negative. It will be seen from the above that I have never once been able to find the tubercle bacillus in the deposit. In four of the five cases lymphocytes were alone found and in one only polymorphonuclear cells. The inoculation test gave a satisfactory result in three out of the four cases and is as yet incomplete in the fourth case. The points of importance in the examination of the spinal fluid are the presence of the tubercle bacillus and lymphocytes in the deposit and the results of the inoculation test. I look upon the cryoscopic and permeability tests as of small significance.

The finding of the tubercle bacillus in the deposit is

by far the best test for clinical purposes. It requires little time. It has given positive results in the hands of various observers up to from half to three-fourths of the cases. I look upon my want of success as a matter of accident. The inoculation test is very valuable but the disadvantage is the delay. Slawyk and Manacatide<sup>46</sup> recommend the injection of four cubic centimetres intraperitoneally. Hellendall<sup>47</sup> advises lumbar inoculation as requiring less fluid. No doubt negative results may be due to the use of too small a quantity of fluid but less quantities than those named above have answered my purpose. It is well, however, to be on the safe side. I take it that, if an acid- and alcohol-fast bacillus resembling the tubercle bacillus is found in the deposit from the spinal fluid obtained from a case with symptoms of meningitis, the nature of that meningitis is determined even should the inoculation test subsequently give a negative result. Therefore I do not quite see the reason for Chipault's<sup>48</sup> hesitation in certainty of diagnosis in a case subsequently to be referred to. The tubercle bacillus may be cultivated from the spinal fluid. Slawyk and Manacatide recommend the use of a fairly large quantity of the fluid for this purpose. Langner (quoted by Hellendall<sup>49</sup>) incubates the fluid at 37° C. and in eight days there is a rapid multiplication of the tubercle bacillus. In one of the cases where I tried this method I obtained a considerable streptococcus growth which I looked upon as a terminal infection. Much has been written lately about lymphocytosis in tuberculous meningitis. It certainly badly misled in Rendu and Gerand's case.<sup>50</sup> Nobécourt and Voisin,<sup>51</sup> Simon,<sup>52</sup> and others have found it in cases of tuberculous tumours without meningitis. They look upon it as a sign of irritation of the membranes. If any polymorphonuclear cells are present as well as lymphocytes a differential count should be made as recommended by Achard and Laubry.<sup>53</sup> Leri<sup>54</sup> pointedly remarks that if the clinical and cyto-diagnosis are not in agreement the cyto-diagnosis is not always right. This applies to one of my cases though fortunately the inoculation

<sup>46</sup> Slawyk and Manacatide : *Berliner Klinische Wochenschrift*, 1898.

<sup>47</sup> Hellendall : *Deutsche Medicinische Wochenschrift*, 1901.

<sup>48</sup> Chipault : *Neurologie Chirurgicale*.

<sup>49</sup> *Loc. cit.*

<sup>50</sup> Rendu and Gerand : *Société Médicale des Hôpitaux*, 1901.

<sup>51</sup> Nobécourt and Voisin : *Société d'Anatomie*, 1903.

<sup>52</sup> Simon : *Revue Mensuelle des Maladies de l'Enfance*, 1903.

<sup>53</sup> Achard and Laubry : *Société Médicale des Hôpitaux*, 1901.

<sup>54</sup> Leri : *Archives de Médecine des Enfants*, 1902.



test settled it. The study of the spinal fluid obviously yields results which are of the first importance in the differentiation of the various forms of meningitis. If aspiration is avoided and the fluid allowed to escape slowly there is no danger in it in meningitis and I see no reason why it should not be used as a routine method in suspected cases of these diseases.

## RECOVERY FROM TUBERCULOUS AFFECTIONS OF THE NERVOUS SYSTEM.

Very occasionally one has the good fortune to meet with recovery from symptoms of grave organic disease of the brain where a tumour has been suspected and syphilis can with almost certainty be excluded. I have notes of two such cases treated in the Leeds Infirmary and possibly of a third. Recovery is often incomplete, blindness remaining. Some great authorities (such as Gowers<sup>55</sup> and others) say that in tuberculous tumours arrest is not uncommon. Presumably some of the recoveries referred to above may be of this nature. It is therefore interesting to inquire what pathological evidence is forthcoming in favour of this view. In two cases from the records of the Leeds Infirmary with healed phthisis there was in one a nodule in the left lenticular nucleus which Dr. Barrs regarded as a healed tuberculous lesion and in the other a calcareous mass of the size of a pea attached to the dura mater. Sufficient proof as to the exact nature of these lesions is not forthcoming. I have only been able to find in literature a few cases of recovery from tuberculous tumours. In Williamson's case<sup>56</sup> there was a small yellowish mass which had caused Jacksonian epilepsy four years previously, in Ashby's case<sup>57</sup> there was a small cyst with cretaceous walls, in Bristowe's case<sup>58</sup> a hard mass was present in the cerebellum, and in Kahlmeyer's case<sup>59</sup> a cicatrix was found in the cerebellum in a man who had cerebellar symptoms 11 years previously. In the first three cases there were other masses in the brain and the patients died from tuberculosis and in the fourth

<sup>55</sup> Gowers : Diseases of the Nervous System, vol. ii.

<sup>56</sup> Williamson : Medical Chronicle, 1896.

<sup>57</sup> Ashby : Diseases of Children.

<sup>58</sup> Bristowe : Brain, 1891.

<sup>59</sup> Kahlmeyer : Berliner Klinische Wochenschrift, 1899.

case there was phthisis. The quiescent lesion showed a dense fibrous capsule in the first three cases. Oppenheim<sup>60</sup> says that these tumours may calcify and then become encapsuled, as if encapsulation were, as it probably is, the most important event. Calcification is nearly always a very limited process in the mass and other encephalitic lesions, as Oppenheim points out, may calcify. By the kindness of the authorities of the London Hospital museum I have looked through a relatively large number of tuberculous tumours but I cannot say that I have seen any which could be regarded as definitely healed. The very slender possibility of recovery from a tuberculous tumour is no doubt established by the above-named cases, but, as Ashby<sup>61</sup> well points out, we must set off against this chance the possible development of other masses in the brain or the child may die from tuberculous meningitis or other form of tuberculosis.

In considering recovery from tuberculous meningitis a distinction must be drawn between the ordinary more generalised form and the limited meningitis *en plaque*. Monnier<sup>62</sup> and others strongly recommend operation for the latter when there are localising symptoms. Gee,<sup>63</sup> in his article on Tuberculous Meningitis, in 1868 graphically described recovery as a matter of science. Many great clinicians have related cases of recovery but up to recently the absolute proof was wanting unless the patient died later, when anatomical demonstration of the healed lesion was provided (Rilliet, Politzer, Barth,<sup>64</sup> Cadet de Gassicourt,<sup>65</sup> Carrington,<sup>66</sup> and others, and more recently Jannsen<sup>67</sup> and Rocaz and Cruchet<sup>68</sup>). Another proof, but not so satisfactory, is the presence of choroidal tubercles controlled by a skilled ophthalmologist (Dujardin-Beaumetz<sup>69</sup> and more recently Thomalla<sup>70</sup>). The presence of an unmistakeable tuberculous lesion such as phthisis elsewhere in the body, as occurred in the cases of Cuffier (quoted by Chante-

<sup>60</sup> Oppenheim : Die Geschwülste des Gehirns, 1896.

<sup>61</sup> Loc. cit.

<sup>62</sup> Loc. cit.

<sup>63</sup> Gee : Reynolds's System of Medicine, 1868.

<sup>64</sup> Barth : Société d'Anatomic, 1879.

<sup>65</sup> Cadet de Gassicourt : Revue Mensuelle des Maladies de l'Enfance, 1884.

<sup>66</sup> Carrington : Transactions of the Pathological Society, 1887.

<sup>67</sup> Jannsen : Deutsche Medicinische Wochenschrift, 1896.

<sup>68</sup> Loc. cit.

<sup>69</sup> Dujardin-Beaumetz : L'Union Médicale, 1879.

<sup>70</sup> Thomalla : Berliner Klinische Wochenschrift, 1902.

messe<sup>71</sup>) and Chappet (quoted by Bouclier<sup>72</sup>), makes the diagnosis almost certain. Mr. E. Ward had a case in the Leeds Infirmary with tuberculous disease of the ankle in which the symptoms of meningitis developed. The child recovered, though unfortunately blind, and is still living.

Bacteriological proof of the nature of the meningitis has been provided in the cases of recovery recorded by Freyhan,<sup>73</sup> Henkel,<sup>74</sup> K. Barth,<sup>75</sup> Gross,<sup>76</sup> and Winkler and Gohl (quoted by Chipault<sup>77</sup>). Tubercle bacilli were found in the spinal fluid in all these cases. The diagnosis in the cases of Rocaz (subsequently anatomically proved by Cruchet<sup>78</sup>), Mottard (quoted by Bouclier<sup>79</sup>), and Sepet,<sup>80</sup> rests on the Courmont-Arloing serum reaction, the value of which is not by any means universally accepted. In his Bordeaux Thesis, 1903, Parrenin states that in October, 1902, the cases of Thomalla, Henkel and Barth were living and well, but that Gross's case had early phthisis; Freyhan's case was quite well when last heard of in 1899.

In inquiring under what conditions recovery has taken place it is only necessary to mention large doses of iodide of potassium, creasote, &c., without confounding cause and effect. Spinal puncture, though possibly of value in a simple meningitis (Hirsch<sup>81</sup>) is of quite doubtful utility in tuberculous meningitis. In the cases of Freyhan, Barth, and of Winkler and Gohl puncture was performed once in each, whereas in the cases of Henkel and Gross the puncture was repeated three times. Chipault<sup>82</sup> is inclined to attribute some value to it, but only a small quantity of fluid was drawn off in the case to which he refers. In Gross's case the patient felt much relieved after it. In my case referred to above, where three punctures were made, 63 cubic centimetres of fluid in all were drawn off but with no real effect. Excess of fluid is not responsible for all the threatening symptoms in tuberculous meningitis, as Peron<sup>83</sup> points out in his experimental investigations. Experi-

<sup>71</sup> Loc. cit.

<sup>72</sup> Loc. cit.

<sup>73</sup> Freyhan: *Deutsche Medicinische Wochenschrift*, 1894.

<sup>74</sup> Henkel: *Münchener Medicinische Wochenschrift*, 1900.

<sup>75</sup> K. Barth: *Ibid.*, 1902.

<sup>76</sup> Gross: *Berliner Klinische Wochenschrift*, 1902.

<sup>77</sup> Loc. cit.

<sup>78</sup> Loc. cit.

<sup>79</sup> Loc. cit.

<sup>80</sup> Loc. cit.

<sup>81</sup> Hirsch: *Wiener Klinische Rundschau*, 1900.

<sup>82</sup> Loc. cit.

<sup>83</sup> Peron: *Archives Générales de Médecine*, 1898.

mentally Martin<sup>84</sup> noted an improvement in a rabbit after withdrawing two cubic centimetres of fluid but it was only temporary. Some of my experiments were made with this object but mostly very little fluid was found. Operations have been undertaken for the relief of this disease by Lannelongue and Keen, quoted by Barlow,<sup>85</sup> Ord and Waterhouse,<sup>86</sup> Parkin,<sup>87</sup> Paget, Kendal Franks,<sup>88</sup> and others. A case under the care of Dr. Churton and Mr. A. W. Mayo Robson<sup>89</sup> has been quoted by some authorities as a possible recovery from tuberculous meningitis, although neither of these authors described it as such. I was resident medical officer at the time this girl was in the Leeds Infirmary and she attended my out-patient room with epilepsy for several years previously to her death which occurred last year. She was trephined on account of focal symptoms which it was thought might be due to abscess secondary to ear disease. The case was obscure and occurred during the influenza epidemic of 1889-90. In her subsequent history she contracted syphilis but never showed any manifestation of tuberculosis.

Notwithstanding the above-mentioned remarkable recoveries from severe tuberculous meningitis, the prognosis must still be looked upon for practical purposes as hopeless. If a benign type of disease really exists systematic examination of spinal fluid should bring it to light. With such a prognosis before us prophylaxis is worthy of the closest attention. The danger which a careless phthisical patient is in his own home has been placed beyond doubt (Cornet,<sup>90</sup> Coates,<sup>91</sup> and others). This danger specially menaces susceptible young children who crawl about the floor stirring up infected dust. The tubercle bacillus is inhaled and a potential infecting focus is established in the bronchial glands. Dieudonné<sup>92</sup> has actually found tubercle bacilli on the hands of children in phthisical homes. Clinical evidence has also furnished some striking examples (Variot<sup>93</sup> and others) in the same direction. The notification of phthisis

<sup>84</sup> Martin : Société de Biologie, 1898.

<sup>85</sup> Barlow : Clifford Allbutt's System of Medicine, vol. vii.

<sup>86</sup> Ord and Waterhouse : THE LANCET, March 10th, 1894, p. 597.

<sup>87</sup> Parkin : THE LANCET, July 1st, 1893, p. 21.

<sup>88</sup> Kendal Franks : Brit. Med. Jour., vol. ii., 1890.

<sup>89</sup> Mayo Robson : Ibid., vol. ii., 1890.

<sup>90</sup> Loc. cit.

<sup>91</sup> Coates : Victoria Thesis, 1901.

<sup>92</sup> Dieudonné : Münchener Medicinische Wochenschrift, 1901.

<sup>93</sup> Variot : Médecine Moderne, 1903.

with disinfection and the isolation in special hospitals of confirmed and careless consumptives (especially if there are young children in their houses) are indispensable steps in the prevention of tuberculous meningitis and general tuberculosis. I am glad to say that we are about to open a hospital of this kind in the centre from which I come.

The old adage that "prevention is better than cure" was never truer than in the case of acute miliary tuberculosis and tuberculous meningitis.















